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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/147,955 | 03/24/99 | MIZUTANI M | 001560-350 |

QZ1839 HZ12/1003
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| EXAMINER |
|---|
| IBRAHIM, M |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1638 | |

**DATE MAILED:** 10/03/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/147,955 | Applicant(s) MIZUTANI ET AL. | |
|---|---|---|---|
| | Examiner Medina Ibrahim | Art Unit 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *8 and 12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11 and 16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-7, 9-11, 16-19, and 20-24, pending in this application, are under examination.

The Response filed on April 16, 2001 has been entered. Applicants should note that clean copy of the amended claims 3-5 are required in response to this Office action.

### *Withdrawn rejections and Objections*

The rejection under 35 USC 112, 2nd paragraphs to claim 2 regarding amino acid modifications, and to claims 2-5 regarding the word "described"; the written description rejection to claims 2-5 and 16-19, the rejection under 35 USC 101 and 102(b) to claim 1 regarding the product of nature, and the rejection under 35 USC 103(a) to claims 1-5 as being unpatentable over Jonsson et al in view of Sambrooke et al, have been withdrawn in view of Applicants' amendment to the claims and arguments filed in the response of 16 April 2001.

### *Objections*

The specification remains objected as the SEQ ID Nos: of the sequence listing submitted on May 12, 2000 are not correlated with the SEQ ID Nos defined in pages 1-4 of the response filed 16 April 2001. Applicants list SEQ ID NO: 2-8, and 12 as amino acids, and SEQ ID NO:1-7, and 11 as the nucleotide sequences. However, SEQ ID NO:1, 3, 5, 7, 9, and 11 define nucleotide sequences, while SEQ ID NO: 2, 4, 6, 8, 10, and 12 are the proteins. The specification should be amended appropriately.

***35 USC § 112, Scope of Enablement***

Claims 1-7, 9-11, and 16-19 remain rejected and new claims 20-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for the isolated sequences of SEQ ID NO: 7 and 9 encoding the plant flavonoid-5-glucosyltransferase (5GT) protein of SEQ ID NO: 8, 10, or 12, plants or plant parts transformed therewith, does not provide enablement for any expressed gene which transfers a glycoside to the 5 position of a flavonoid, or any isolated gene or a nucleotide sequence that hybridize thereto, or its complementary strand, coding for a protein having 5GT activity or homologous sequences having 30%-50% amino acid identity with SEQ ID NO: 8, 10 or 12, a modified protein thereof having one or more amino acid additions, and/or deletions, and/or substitutions that maintain flavonoid-5-glucotransferase activity. This rejection is repeated for the same reasons of record as set forth in the office action mailed on 10/16/00. Applicant's arguments filed on 16 April 2001 have been fully considered but they are not persuasive.

Applicants traverse, in pages 4-5, that based on the description from the specification, the significant degree of homology of 5GT proteins between different species, one skilled in the art can identify and clone other genes from other sources using conventional hybridization technique. Applicants assert that no undue experimentation would be necessary to practice the invention. These arguments are not found persuasive for the same reasons set forth in pages 4-6 of the last office action. Applicants have provided no evidence that genes of the claimed invention obtainable by conventional hybridization will encode a functional protein since no primers specific

for 5GT genes have been disclosed. To isolate and screen all known and unknown protein encoding genes for the ability to transfer a glycoside to the 5 position of a flavonoid without guidance as to how inoperable embodiments can be eliminated without undue experimentation is an invitation to experiment. Regarding Applicant's argument (page 9, 2nd full paragraph) that, in Kossman et al article, the cDNA of a dicot plant was cloned using SSS I of a monocot plant is not persuasive because the sources of the instantly claimed genes are not limited to related plant species or families but encompass any 5GT gene from a wide variety of plant species. Furthermore, the claims encompass genes encoding proteins having as low as 30% -50% sequence identity to the disclosed protein or genes that hybridize with all or a portion of a nucleotide sequence encoding SEQ ID NO: 8, 10 or 12 under mild hybridization conditions, in which their ability to encode proteins having 5GT activity is questionable. For example, Bandurski et al ( attached Sequence Search Results, page 1, see page 1, Accession no. Q41819) teach a gene from *Zea mays* encoding a non-5GT protein with 35% of overall and local similarity to SEQ ID NO:12. The claims also encompass genes encoding SEQ ID NO:8, 10 or 12 comprising deletions and/or additions and/or substitutions of one or more amino acid sequences that still retains 5GT activity. The working examples given in the specification are limited to unmodified SEQ ID NO: 7 or 9 and unmodified SEQ ID NO: 8, 10, or 12. The specification provided no guidance as to which region in the disclosed protein can be modified by deletions and/or additions and/or substitutions so that the protein activity is unchanged. The state of the prior art teaches unpredictability in protein function following amino acid modifications. For example, Broun et al

(Science, 13 November 1998, Vol. 282, pp. 131-133 (U)) teach that as few as four amino acid substitutions can change an oleate 12-desaturase activity (Abstract). See also Lazar et al (Molecular and Cellular Biology, March 1988, Vol. 8, No. 3, pp. 1247-1252 (V) ) who teach that a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor alpha results in different biological activities (Title). Therefore, it is unclear whether the protein modifications of claims 2-4 and 24, or the gene modifications of claims 5, 20, 22-24, would result functional 5GT proteins/genes. Accordingly, one of skill in the art would not be able to practice the invention as broadly claimed without undue experimentation, as stated in the last office action.

Furthermore, analogous to Amgen Inc. V. Chugai Pharmaceutical Co. Ltd, which was disclosed in page 6 of the last office action, the disclosure of a few unmodified sequences encoding unmodified protein having 5GT activity does not enable claims broadly drawn to genes encoding proteins having as low as 30% -50% sequence identity to the disclosed protein or genes that hybridize with all or a portion of genes encoding SEQ ID NO: 8, 10, or 12 under mild hybridization conditions or genes encoding mutated proteins that retain 5GT activity.

The rejection is made and maintained.

***Written Description***

Claims 1, 6-7, 9-11, remain rejected and new claims 20-21, and 23 are rejected under 35 U.S.C 112, first paragraph, as the specification does not provide an adequate written description of the invention as broadly claimed. This rejection is repeated for the same reasons of record as

set forth in the office action mailed on 10/16/00. Applicants' arguments filed on 16 April 2001 have been fully considered but they are not persuasive.

Applicants assert that given the description of the genus of the 5GT gene, the particular cDNAs described in the specification, the significant degree of homology in the proteins between different plant species, and the ability of one skilled in the art to use the information provided to identify additional 5GT genes, one skilled in the art would recognize that the inventors had possession of the invention as claimed. These arguments are not persuasive because the specification does not disclose a representative species of the claimed genus which will allow one skilled in the art to predict with a reasonable certainty the structure of other species within the genus. Claims 1, 20, and 23, part (I) recite isolated genes or nucleic acid molecules encoding a protein having a plant flavonoid-5-glucosyltransferase (5GT) activity. Applicants disclose SEQ ID NO: 7 and 9, or nucleic acid molecule encoding 8, 10, or 12 . The claims encompass 5GT genes from other plant sources. This is precisely the situation the court in Lilly which held that a disclosure of one or several species does not provide adequate Written Description for all species in the genus. There is no known or disclosed correlation between the DNA structure and the activity of 5GT which would allow one skilled in the art to predictably determine what will be the structure of the non-described sequences. Nor does the specification discloses consensus sequences common to all plant 5GT proteins/genes. Claim 21 is drawn to 5GT genes from *Perilla, torenia, verbena and petunia* . The claim reads on allelic variants and mutants of *Perilla, torenia, verbena and petunia* 5GT genes which Applicant was not of possession at the time of

filing. The claim implies that other Perilla, torenia, verbena and petunia 5GT genes, other than the disclosed sequences exist in nature , but the structures thereof are not known. Thus, there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such an allelic variants or mutants, absent further guidance. Since there is no evidence that Applicant was in possession of the claimed 5GT genus, Applicants are not in possession of the claimed process of claim 9 and the plants and plant parts of claims 10-11. Accordingly, there is lack of adequate description to inform a skilled artisan that Applicant was in possession of the claimed invention at the time of filing. See, Written Description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

***35 USC § 112, 2nd paragraph***

Claims 1-7, 9-11, 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants should note that the claims are replete with vague and indefinite terms, as well as typographical errors. For example, SEQ ID NO:7-10 and 12 are claimed as amino acid sequences in claims 2-5, and 24, and as nucleotide sequences in claims 22-23. Careful and complete review of all claims are suggested.

In claims that recite "gene", gene implies a DNA sequence that exists in nature and includes coding, non-coding regions, as well as all regulatory sequences associated with expression. This does not appear to be Applicant's intention, as evidenced by Applicant's

recitation of "isolated" . It is suggested that Applicant amend "gene" to ----DNA--- or ---nucleic acid molecule---.

Claims 3-4, 22 and 24 recite "% of homology", it is unclear as to how the homology has been assessed. Is it functional or structural homology? It is suggested that " homology" be replaced with ---sequence identity--- for clarification.

Claim 5, recites "can be hybridized" which implies the claimed sequence can or cannot be hybridized with SEQ ID NO:7 or 9. Applicants should note that SEQ ID NO: 8, 10, and 12 are amino acid sequences. It is suggested that "can be hybridized" be replaced with ---hybridizes----, for clarification.

Claims 10-11 and 16-19 remain indefinite in the recitation of "identical properties", as it is unclear what properties are identical and what properties are not identical. The metes and bounds of the claims are unclear. If Applicants intend to claim "progeny or tissues that retain the gene which was introduced into the parent plant" the claims should be recited as such.

In claim 19, "breeding" should be deleted as it renders the process incomplete, since the essential breeding steps are missing.

In claim 20, "A isolated" should be changed to ---An isolated---. The second comma should be placed after "sequence encoding".

Claims 2-5 and 24 drawn to an isolated gene coding amino acid sequences of SEQ ID NO:7-10 and 12 are indefinite because SEQ ID NO:7 and 9 are nucleotide sequences, not amino acid sequences. Claim 24, lines 7-8, is confusing in the recitation of "amino acid sequence which

will hybridize with a complementary strand of an amino acid sequence of SEQ ID NO: 7-10 and 12. Amino acid sequences do not hybridize. Appropriate correction is required. Dependent claims 16-19 are included in the rejection.

In claim 24, line 3, "those shown in" should be deleted for clarification.

Claims 22-23, drawn to nucleotide sequence complementary or hybridizes with nucleotide sequence of SEQ ID NO:7-10 and 12 are indefinite because SEQ ID NO: 8, 10 and 12 are amino acid sequences, not nucleotide sequences. Appropriate corrections are required.

***Claim Rejections - 35 USC § 102***

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Brugliera et al (US 5,859,334, filed March 1995(A)).

The claims are drawn to an isolated nucleotide sequence complementary to or that hybridizes to a sequence encoding a plant 5GT including SEQ ID NO:7-10 and 12. The nucleotide sequences encompasses sequences that are not fully complementary to SEQ ID NO: 7 and 9 and which read on as few as 2-mers , said 2-mers would also hybridize with SEQ ID NO:7 and 9. Applicants should note that SEQ ID NO: 8, 10 and 12 are protein sequences.

Brugliera et al teach an isolated nucleotide sequence encoding a Petunia 3RT protein, said nucleotide sequence would inherently comprise the claimed " complementary" sequence which includes sequences that are not fully complementary and which read 2-mers, said 2-mers will hybridize to SEQ ID NO: 7 or 9.

***Claim Rejections - 35 USC § 103***

Claims 1-7, 9-11, and 16-19 remain rejected, and new claims 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brugliera et al (US 5,859,334, filed March 1995) in view of Jonsson et al and Sambrooke et al. This rejection is repeated for the same reasons of record as set forth in the office action mailed on 10/16/00. Applicants arguments filed on 16 April 2001 have been fully considered but they are not persuasive.

Applicants argue that instant claims are not obvious over the cited references because Brugliera et al teach 3RT genes and merely refers to a 5GT gene, but do not teach an isolated 5GT gene. Nor does the combination of Jonsson et al and Sambrooke remedy the deficiency of Brugliera et al. Therefore, the rejection should be withdrawn. These arguments are not persuasive because the claims are not limited to specific sequences of 5GT genes but broadly drawn to isolated genes or nucleic acid sequences, partially complementary or hybridizing sequences thereof from any plant source encoding a protein having 5GT activity as well as protein modified by deletions and/or additions and/or substitutions of one or more amino acid sequences that still retains 5GT activity, homologous sequences having 30% to 50% or more sequence identity to the disclosed sequences, and transgenic plants/plant parts having identical properties.

Contrary to Applicants' assertion, Brugliera et al not need to teach isolated 5GT gene because under 35 USC 103, all that is required is to establish a prima facie case of obviousness. Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so

found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Brugliera et al teaches isolation, sequencing and cloning of 3RT (a related gene), process for producing purified plant 3RT protein, and transformed plants/plant parts expressing said protein, and suggest an isolated nucleotide sequence encoding a plant flavonoid 5-O-glucosyltransferase, as stated in the last office action. While Brugliera does not disclose isolated and purified 5GT sequences, one of ordinary skill in the art would be motivated to use a 5GT gene with the process disclosed by Brugliera et al, given the importance and availability of the 5GT gene disclosed by Jonsson and Sambrooke to produce transformed plants or plant parts, like cut flowers, with desired phenotype, or for the production of 5GT protein as taught by Brugliera et al, with reasonable expectation of success. In column 3, lines 30-36 Brugliera suggests a nucleotide sequence complementary to a nucleotide sequence encoding a 5GT; homologous sequences of the disclosed 3RT sequences; in columns 7-8, protein mutations comprising amino acid substitution, additions, and/or deletions are also disclosed. Therefore, the claimed invention as whole was clearly *prima facie* obvious.

Furthermore, Applicants' evidence of unexpected results, namely, isolated nucleic acid sequence of SEQ ID NOs: 7 and 9 or the nucleotide sequence encoding SEQ ID NO:8, 10, or 12 or a method of their use to obtain transformed plant/ plant parts is not commensurate with the scope of the claims which encompass nucleotide sequences, their complements, sequences hybridizing under mild hybridization conditions to the disclosed sequences or non-disclosed

sequences, still encoding plant 5GT proteins or homologous sequences thereof having 30%-50% identity, or modified proteins thereof that retains 5GT activity or plant/plant parts comprising it. See *In re Lindner*, 173 USPQ 356 (CCPA 1972) and *In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of unexpected results should be commensurate with the scope of the claims.

No claim is allowed.

Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday -Tuesday 8:30 AM to 4:30 PM, and Wednesday-Thursday from 9:00AM to 3:00 PM

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

September 14, 2001
mai

PHUONG T. BUI
PRIMARY EXAMINER